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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,132	08/06/2001	Gary S. Saylor	6704-15-1	8944
7590	10/21/2003			
BARBARA S. KITCHELL AKERMAN, SENTERFITT & EIDSON, P.A. 222 Lakeview Avenue, Fourth Floor P.O. Box 3188 West Palm Beach, FL 33402-3188			EXAMINER LAMBERTSON, DAVID A	
			ART UNIT 1636	PAPER NUMBER

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,132	SAYLER ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13,15-20 and 23-27 is/are pending in the application.
- 4a) Of the above claim(s) 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13,15-20 and 24-27 is/are rejected.
- 7) ☒ Claim(s) 23 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>1003</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5,11</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-3, 5-6 and 8-27, as they regard a method and device for detecting the analyte mercury) in the response filed July 17, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Acknowledgement is made of a preliminary amendment filed March 7, 2003 that was inadvertently not considered with respect to the Restriction/Election requirement mailed June 17, 2003. The amendment was not matched with the file wrapper until after the mailing of the Restriction/Election requirement, but has now been entered and considered.

Claims 1-13, 15-20 and 23-27 are pending in the instant application. Claims 14, 21 and 22 were cancelled in the amendment filed March 7, 2003. Claim 7 has been rejoined to the elected invention in view of the preliminary amendment because it now depends specifically from an elected claim.

Claim 4 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed July 17, 2003.

Claims 1-3, 5-13, 15-20 and 23-27 are ready for examination with respect to a device for the detection of the analyte mercury.

Priority

Applicant's claim for domestic priority to US Application No. 60/225,232 under 35 U.S.C. 119(e) is acknowledged. However, the first line of the specification refers to the provisional application as a continuation-in-part. This reference is improper because a provisional application cannot be related to a non-provisional application as either a continuation, divisional or continuation-in-part. The reference must be amended appropriately.

Information Disclosure Statement

The information disclosure statements filed September 16, 2002 and January 15, 2002 have been considered, and a signed and initialed copy of the form PTO-1449s are attached to this Office Action. Reference A1 has been indicated as document 5,571,722, as this is the only document labeled "A1" in the references submitted by applicant.

Claim Objections

Claim 8 is objected to because of the following informalities: the claim contains the term "*P. fluorescens*" which is an abbreviation; it is appropriate to completely spell out all abbreviations upon their first appearance in the claims. Appropriate correction is required.

Claim 23 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot be dependent on another multiply-dependent claim. See MPEP § 608.01(n). In this particular instance, claim 19 is multiply-dependent on claims 2 or 3, while claim 23 is multiply-dependent on claims 19 or 20. Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a device for the detection of *any* analyte, in some embodiments specifying the use of a particular regulatory element (*merRo/p*) to detect these analytes. The claims read on a device for the detection of a broad genus of analytes, many of which cannot readily be detected by the specific *merRo/p* element disclosed in the specific embodiments of the claimed device.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

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Applicant claims a device for the detection of *any* analyte by function only, without any disclosed or known correlation between the regulatory elements required to detect these analytes and their ability to detect any analyte. The important element to this device is the regulatory element that is responsive to a particular analyte. The specification does provide teachings regarding the detection of certain analytes (i.e., mercury, naphthalene, toluene, etc.) using very specific regulatory elements that are separately responsive to each of these particular analytes. However, each of these regulatory elements has a different structure-function relationship, evidenced by the fact that each regulatory element is responsive only to the particular analyte that it detects (e.g., *merRo/p* is responsive to mercury, *nahRG* is responsive to naphthalene, etc.). In other words, the *merRo/p* element is sufficient to detect mercury, but is insufficient to detect other analytes such as naphthalene, toluene, etc., because *merRo/p* has a particular structural feature that allows the function detection of mercury. Thus, there is no particular structure-function relationship disclosed between the disclosed analyte-detecting regulatory elements that would allow the skilled artisan to readily envision other analyte-detecting regulatory elements, as well as the particular analytes that would elicit a responsive action from each regulatory element. This is because each regulatory element has a specific structural characteristic that confers an ability to respond to a particular analyte. Thus, the skilled artisan cannot envision a sufficient number of regulatory elements that can detect *any* analyte because there is no common structural element between the disclosed analyte-detecting regulatory elements that would allow the skilled artisan to readily identify another analyte-detecting regulatory element and its cognate response-eliciting analyte.

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The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of analyte-detecting regulatory elements by disclosing structural or functional features of analyte-detecting regulatory elements so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of analyte-detecting regulatory elements such that the skilled artisan can envision any particular analyte-detecting regulatory element, and which analyte would elicit a responsive action from that regulatory element. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 9, 24 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the strain *P. fluorescens* 5R, ARL1, ARL2 and ARL3 are required to practice the invention. As such, the strains must be readily available or obtainable by a

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repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the strains. In the instant case, the process to generate the strains that is disclosed in the specification does not appear to be repeatable, nor does it appear the strains are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

- a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
- b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;
- c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;
- d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and
- e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites the limitation "said bioreporter bacterium" in lines 6-7 of the claim. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to amend the claim to read, "said stably transformed bioreporter bacterium."

Claim 25 recites the limitation "A mobile method for detecting mercury..." The nature of this limitation is unclear because the nature of the mobility of the method is not readily discernible within the claim. In other words, it is unclear if the method itself is mobile, or if there is an element within the method that is mobile (i.e., is there a device that is mobile).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 10-13, 15-17, 19, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Lyngberg *et al.* (IDS reference C-13; see entire document; henceforth Lyngberg). Also, see the Table of Contents supplied by the examiner to establish the date of public availability as August 12, 1999.

Lyngberg teaches a single-use Hg(II) (i.e., divalent mercury) patch biosensor device/apparatus comprising bacteria (specifically *E. coli*) that express a luciferase gene that has been operably linked to a mercury-sensitive regulatory element (e.g., an operator), where the bacteria is immobilized/encapsulated in a latex polymer matrix (see for example the Abstract, page 668-669, the bridging paragraph). A diagram of the device/apparatus containing the biosensor is provided in Figure 2 (see for example page 670), where it is clearly shown that the immobilized bacteria are attached to a polyester support matrix. The small nature of the device/apparatus indicated in Figure 2 (the apparatus is only approximately 15mm in length) inherently confers the property that it can be carried by hand. The mercury-sensitive regulatory element that is used is the *merRo/p* (i.e., o/p indicates the presence of both the operator and promoter) element (see for example Figure 1 on page 669), which is the same element indicated in the instant invention. The particular bioluminescent reporter gene that is used is the *luxCDABE* gene cluster (see for example Figure 1 on page 669), which is also the same reporter gene indicated in the instant invention. These elements are incorporated into the bacteria on a plasmid, such as pRB28 (see for example Figure 1, page 669). This construct allows the identification of divalent mercury in a sample because the divalent mercury activates the expression and resulting activity of the bioluminescent lux gene product. The lux gene product can be detected using film (see for example page 668, right column first full paragraph), thus a camera or other film-containing device can serve as a portable detection device. Additionally, according to the specification, the lux gene emits visibly detectable light (see for example page 5, lines 18-19 of the instant specification), thus the human eye can also serve as a portable detection device. Since Lyngberg teaches all of the elements set forth in the device/apparatus,

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Lyngberg must also inherently teach the genetically modified bacterium present in the apparatus.

Finally, an anticipated use for the device is the detection of divalent mercury in water samples (see for example page 668, left side, first full paragraph) as a less expensive alternative to chemical methods.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 5 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Simpson *et al.* (US 6,117,643; see entire document; henceforth Simpson).

Simpson teaches a bioluminescent bioreporter integrated circuit (i.e., an apparatus/device) that is useful for the detection of heavy metals samples such as water (see for example the Abstract). The bioreporter comprises a genetically modified microorganism such as a bacterial strain, where the bioreporter is either integrated into the chromosome of the organism, or maintained on plasmids (see for example column 1, lines 25-35). In a specific embodiment of the invention, the bacterium used in the bioreporter is a *Pseudomonas fluorescens* strain (see for example column 3, lines 15-32). The bacterium is encapsulated in a polymer matrix to keep the

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bioreporter in proper position with respect to a photodetector (see for example column 8, lines 32-39), which is a portable detection device. The device, overall, is considered by Simpson to be a portable detection device (see for example column 2, lines 7-22 and column 14, lines 59-64). Significantly, Simpson indicates that a preferred bioreporter to be used in the biosensor is the *Vibrio fischerii luxCDABE* gene product (see for example column 23, lines 20-23), which can be linked to a promoter that is responsive to an environmental factor (see for example column 23, line 65 to column 24 line 18). Importantly, Simpson references the ability to detect environmental factors such as Hg(II) by placing the promoter of interest in front of the promoterless lux genes from *Vibrio fischerii* (see for example column 1 line 63 to column 2, line 5).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 3, 6-8, 10-13, 15-17, 19-20, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson as applied in the rejection of claims 1, 5 and 8 under 35 USC § 102(e) above, in view of Lyngberg (IDS reference C-13) as applied in the rejection of claims 1-3, 5-7, 10-13, 15-17, 19, 25 and 27 under 35 USC § 102(b).

Simpson teaches all of the elements as indicated above in the rejection of claims 1, 5 and 8 under 35 USC § 102(e). Simpson does not specifically teach the use of the *merRo/p* regulatory

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element in their apparatus, although Simpson references the ability to detect its inducer (Hg(II)) by placing the promoter element in front of a promoterless lux gene. Similarly, Simpson does not teach the particular bacterium comprising the *merRo/p* regulatory element operably linked to the lux gene, or method of using said bacterium when placed in their device/apparatus.

Lyngberg teaches all of the elements as set forth above in the rejections of claims 1-3, 5-7, 10-13, 15-17, 19, 25 and 27 under 35 USC §102(b). Specifically, Lyngberg teaches the use of the *merRo/p* regulatory element in the bacterium used in their apparatus, as well as the particular bacterium and method of using said bacterium to detect divalent mercury in samples.

It would be obvious to combine the teachings of Simpson and Lyngberg because both teachings involve the use of an apparatus, comprising a bacterium expressing a promoterless lux gene under the control of a regulatory element, to detect the presence of an analyte, particularly mercury as suggested by Simpson and specifically taught by Lyngberg. The ordinary skilled artisan would have been motivated to combine the teachings because Simpson suggests using their apparatus to detect divalent mercury, while Lyngberg provides the clear teachings of a divalent mercury-responsive regulatory element operably linked to a lux reporter gene for the express use in the detection of divalent mercury in water samples; thus the teachings of Lyngberg reduce to practice a suggested embodiment of the teachings of Simpson.

Absent evidence to the contrary, the skilled artisan would have had a reasonable expectation of success when practicing the claimed invention.

Claims 13 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyngberg as applied to claims 1-3, 5-7, 10-13, 15-17, 19, 25 and 27 under 35 USC §102(b), in view of Lommi *et al.* (US 5,635,368; see entire document; henceforth Lommi).

Lyngberg teaches all of the elements as set forth above in the rejections of claims 1-3, 5-7, 10-13, 15-17, 19, 25 and 27 under 35 USC §102(b). Specifically, Lyngberg teaches the use of the *merRo/p* regulatory element operably linked to a lux reporter gene in a bacterium, and the attachment of said bacterium to a support matrix. However, Lyngberg does not specifically teach attaching the bacterium to a cellulose support.

Lommi provides general teachings of immobilizing (i.e., attaching) a bacterium to a cellulose support matrix, indicating that cellulose has the advantage of trapping the bacteria by a means of solvent precipitation.

It would have been obvious to combine the teachings of Lyngberg with those of Lommi because cellulose is an adequate support matrix for the immobilization of bacteria, as taught by Lommi. The ordinary skilled artisan would have been motivated to combine the teachings in order to have the advantage of being able to immobilize their bacteria by solvent precipitation, as taught by Lommi.

Absent evidence to the contrary, the skilled artisan would have had a reasonable expectation of success when practicing the claimed invention.

Allowable Subject Matter

No claims are allowable.

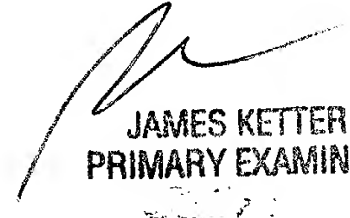
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
AU 1636



JAMES KETTER
PRIMARY EXAMINER